UNITED STATES *v.* GENERIX DRUG CORP. ET AL.

CERTIORARI TO THE UNITED STATES COURT OF APPEALS FOR THE ELEVENTH CIRCUIT

No. 81–1222. Argued November 3, 1982—Decided March 22, 1983

The Federal Food, Drug, and Cosmetic Act (Act) prohibits the marketing of a "new drug" without the prior approval of the Food and Drug Administration (FDA). Section 201(p) of the Act defines a "new drug" as "any drug . . . [which] is not generally recognized . . . as safe and effective . . . or . . . which has not, otherwise than in [safety and effectiveness] investigations, been used to a material extent or for a material time." Section 201(g)(1) defines the term "drug" as, *inter alia*, "articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or in other animals." The Government brought an action in Federal District Court to enjoin respondent Generix Drug Corp. (respondent) from distributing a number of generic drug products containing specified active ingredients, alleging that the FDA had never approved "new drug" applications with respect to such products. Holding that a generic drug product containing the same active ingredients as a previously approved pioneer drug marketed under a brand name is a "new drug" if there is a reasonable possibility that the differences in inactive "excipients" between the generic product and the pioneer drug will make the generic product less safe and effective, and finding that the Government had established a reasonable possibility that the safety and effectiveness of respondent's generic drug products might be affected by differences between their inactive "excipients" and those found in approved products, the court enjoined respondent from distributing the products in question. The Court of Appeals vacated the injunction and remanded with instructions to dismiss the complaint, holding that the statutory prohibition against the sale of a "new drug" without prior FDA approval does not apply to a drug product having the same active ingredients as a previously approved drug product, regardless of any differences in "excipients."

Held: A generic product is a "drug" within the meaning of the indicated definition in § 201(g)(1). That definition is broad enough to encompass entire drug products, complete with their active and inactive ingredients. Accordingly, a generic drug product is a "new drug," subject to prior FDA approval, until the product (and not merely its active ingredients) no longer falls within the terms of § 201(p). Pp. 457–461.

654 F. 2d 1114, reversed.

STEVENS, J., delivered the opinion for a unanimous Court.

Jerrold J. Ganzfried argued the cause for the United States. With him on the briefs were *Solicitor General Lee, Assistant Attorney General Baxter, Deputy Solicitor General Claiborne, John J. Powers III, Nancy C. Garrison,* and *Jeffrey B. Springer.*

Robyn Greene argued the cause and filed a brief for respondents.*

JUSTICE STEVENS delivered the opinion of the Court.

The question presented is whether the statutory prohibition against the marketing of a "new drug" without the prior approval of the Food and Drug Administration (FDA) requires respondent Generix Drug Corp. to have approved new drug applications (NDA's) before it may market its generic drug products. In statutory terms, we are required to determine whether the term "drug" as used in the relevant sections of the Federal Food, Drug, and Cosmetic Act (Act), as amended, 21 U. S. C. § 301 *et seq.* (1976 ed. and Supp V), refers only to the active ingredient in a drug product or to the entire product. We hold that Congress intended the word to have the broader meaning.

I

The active ingredients in most prescription drugs constitute less than 10% of the product; inactive "excipients" (such as coatings, binders, and capsules) constitute the rest. The term "generic drug" is used to describe a product that contains the same active ingredients but not necessarily the same excipients as a so-called "pioneer drug" that is mar-

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*Briefs of *amici curiae* urging reversal were filed by *Joel E. Hoffman* and *Robert M. Lichtman* for the Pharmaceutical Manufacturers Association; by *Richard Ayres Givens* for the Generic Pharmaceutical Industry Association; and by *Michael R. Sonnenreich, Michael X. Morrell,* and *William H. Kenety* for Medicine in the Public Interest.

Clark M. Clifford, Robert A. Altman, and *Daniel F. O'Keefe, Jr.*, filed a brief for the Proprietary Association as *amicus curiae.*

keted under a brand name.[1] Respondent Generix is a distributor of generic drugs manufactured by other firms.

The Government initiated this action to enjoin Generix from distributing in interstate commerce a number of generic drug products that contain eight specified active ingredients.[2] It alleged that the FDA had never approved new drug applications with respect to any of those products.[3]

The District Court held that a generic drug product containing the same active ingredients as a previously approved pioneer drug is a "new drug," requiring an NDA, only if there is a reasonable possibility that the differences in excipients between the generic product and the pioneer will make the generic product less safe and effective. 498 F. Supp. 288, 292. The court found clear evidence in support of the general proposition that differences in excipients may affect the safety and effectiveness of drug products. Excipients may affect the rate at which the active ingredient is delivered to a diseased organ. If delivery is too fast, the patient may be harmed just as if he received an overdose; if delivery is too slow, the treatment of the disease may be ineffective. *Id.*, at 291.

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[1] Generic drugs, also called "copycat" or "me-too" drugs, are usually marketed at relatively low prices because their manufacturers do not incur the research, development, and promotional costs normally associated with the creation and marketing of an original product.

[2] The eight ingredients were: allopurinol, spironolactone with hydrochlorothiazide, furosemide, diethylpropion hydrochloride, chlorothiazide with reserpine, amitriptyline with perphenazine, prochlorperazine maleate, and chlorthalidone. The District Court explained the use of each of these ingredients, noting that furosemide is one of the most widely used drugs in the United States, it being used to treat hypertension and edema. 498 F. Supp. 288, 289–290.

[3] Section 505(a) of the Act, 52 Stat. 1052, as amended, 76 Stat. 784, 21 U. S. C. § 355(a), provides:

"(a) Necessity of effective approval of application

"No person shall introduce or deliver for introduction into interstate commerce any new drug, unless an approval of an application filed pursuant to subsection (b) of this section is effective with respect to such drug."

In this case, the District Court found that the Government had established a reasonable possibility that the safety and effectiveness of six of respondent's generic drug products might be affected by differences between their excipients and those found in approved products.[4] Accordingly, it enjoined the defendants from further distribution of products containing the designated active ingredients.

The Court of Appeals for the Fifth Circuit, now the Eleventh Circuit, vacated the District Court's injunction and remanded with instructions to dismiss the complaint. 654 F. 2d 1114. It held that the statutory prohibition against the sale of a "new drug" without prior approval does not apply to a drug product having the same active ingredients as a previously approved drug product, regardless of any differences in excipients. It based that conclusion on its view that the statutory requirement of evaluating the safety and effectiveness of new drugs must normally relate to active ingredients, because the precise technique of formulating the finished drug is not part of the information generally known to the medical or scientific community. Moreover, it believed that the legislative history suggested that Congress had not intended to create a product-by-product licensing system. Since the active ingredients at issue had all received the necessary approval, the Court of Appeals concluded that the Government was entitled to no relief at all.

Because the question is obviously important and because it has been decided differently in other Circuits,[5] we granted certiorari. 455 U. S. 988.[6]

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[4] Since no evidence concerning the safety and effectiveness of formulations containing prochlorperazine maleate or chlorthalidone was presented at the hearing, no relief was granted with respect to products containing those ingredients. 498 F. Supp., at 294.

[5] *Premo Pharmaceutical Laboratories, Inc.* v. *United States*, 629 F. 2d 795 (CA2 1980).

[6] Respondent Generix has argued that the case is moot because almost its entire store of products containing the disputed active ingredients is no longer salable, and in the future it intends only to sell generic drugs that

II

In resolving the narrow issue presented, the Court of Appeals misread the statutory text.

Section 201(p) of the Act defines a "new drug" to be "any drug . . . [which] is not generally recognized . . . as safe and effective . . . or . . . which has not, otherwise than in [safety and effectiveness] investigations, been used to a material extent or for a material time . . . ."[7] The Court of Appeals did not rest its decision on a finding that Generix's products are generally recognized as safe and effective; rather, its conclusion rested on the proposition that the statutory phrase "any drug" does not include a complete drug product, but only an active ingredient. That proposition is simply untenable.

The original Federal Food and Drugs Act of June 30, 1906, 34 Stat. 768, prohibited the sale of adulterated or misbranded

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have FDA approval. The possibility that respondent may change its mind in the future is sufficient to preclude a finding of mootness. See *City of Mesquite* v. *Aladdin's Castle, Inc.*, 455 U. S. 283, 288–289 (1982); *United States* v. *W. T. Grant Co.*, 345 U. S. 629, 632 (1953).

[7] The full text of § 201(p), 52 Stat. 1041–1042, as amended, 76 Stat. 781, 21 U. S. C. § 321(p), reads as follows:

"The term 'new drug' means—

"(1) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug is not generally recognized, among experts qualified by scientific training and experience to evaluate the safety and effectiveness of drugs, as safe and effective for use under the conditions prescribed, recommended, or suggested in the labeling thereof, except that such a drug not so recognized shall not be deemed to be a 'new drug' if at any time prior to June 25, 1938, it was subject to the Food and Drugs Act of June 30, 1906, as amended, and if at such time its labeling contained the same representations concerning the conditions of its use; or

"(2) Any drug (except a new animal drug or an animal feed bearing or containing a new animal drug) the composition of which is such that such drug, as a result of investigations to determine its safety and effectiveness for use under such conditions, has become so recognized, but which has not, otherwise than in such investigations, been used to a material extent or for a material time under such conditions."

foods or drugs. The definition of the term "drug" in that statute was plainly broad enough to describe a completed drug product. It provided:

> "That the term 'drug,' as used in this Act, shall include all medicines and preparations recognized in the United States Pharmacopoeia or National Formulary for internal or external use, and any substance or mixture of substances intended to be used for the cure, mitigation, or prevention of disease of either man or other animals." 34 Stat. 769.

In 1938, Congress passed the new statute, which requires that an application be submitted to the FDA before any "new drug" may be introduced into interstate commerce. Federal Food, Drug, and Cosmetic Act of 1938, 52 Stat. 1040, 21 U. S. C. § 301 *et seq.* (1976 ed. and Supp. V). The new Act's definition of the term "drug" is even broader than the old one:

> "[201](g)(1) The term 'drug' means (A) articles recognized in the official United States Pharmacopoeia, official Homoeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them; and (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals; and (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals; and (D) articles intended for use as a component of any article specified in clauses (A), (B), or (C) of this paragraph; but does not include devices or their components, parts, or accessories." 52 Stat. 1041, as amended, and as set forth in 21 U. S. C. § 321(g)(1).

In examining this statutory definition, the Court of Appeals was persuaded that only active ingredients come within the terms of subsection (A). 654 F. 2d, at 1116.[8] Unfortu-

[8] But cf. The United States Pharmacopeia 2 (20th rev. ed. 1980) ("article" is an item for which a monograph exists; monographs may exist for the

nately, the court did not analyze the entire definition. If it had done so, it would have noted both that the terms of subsections (A), (B), and (C) are plainly broad enough to include more than just active ingredients, and that they *must* do so unless subsection (D) is to be superfluous. Because the definition is disjunctive, generic drug products are quite plainly drugs within the meaning of the Act.

The natural reading of this definition is corroborated by other sections of the Act. Section 501(a) provides that a "drug" is deemed adulterated "if [it is a drug which] bears or contains, for purposes of coloring only, a color additive which is unsafe." 52 Stat. 1049, as amended, 21 U. S. C. § 351(a)(4). Section 502(e) provides that a "drug . . . fabricated from two or more ingredients" shall be deemed to be misbranded unless its label includes, "whether active or not, the established name and quantity or proportion of any bromides, ether, chloroform, [etc.]." 52 Stat. 1050–1051, as amended, 21 U. S. C. § 352(e)(1). And § 505(b) requires that an application for new drug approval contain "a full list of the articles used as components of such drug [and] a full statement of the composition of such drug." 52 Stat. 1052, 21 U. S. C. § 355(b). . The term "drug" is plainly intended throughout the Act to include entire drug products, complete with active and inactive ingredients.[9]

Neither the Court of Appeals nor respondents have pointed to anything in the text of the Act that is inconsistent

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"finished, or partially finished . . . preparation or product of one or more official substances [active ingredients or excipients] formulated for use on or for the patient").

[9] At oral argument, respondents suggested that it would be nonsensical to understand the word "drug" in § 502(i) of the Act, 52 Stat. 1051, 21 U. S. C. § 352(i), to mean "drug product," because any generic drug is "an imitation of another drug." Tr. of Oral Arg. 41–42. But § 502(i) is intended to prohibit a company from passing an imitation off as the original; if "imitation" is understood with that in mind, it becomes apparent that the word "drug" can and should mean "drug product" in § 502(i), as well.

with our reading of its plain language.[10] The respondents make a number of arguments based upon legislative history and administrative practice regarding the marketing of generic prescription and over-the-counter drugs that lend support to the proposition that two products need not have precisely the same molecular structure in order to be the same "drug."[11] None of those arguments, however, warrants the conclusion that the term "drug" means only the active ingredient in a product.

In this case we are not required to determine what types of differences between drugs would be significant or insignificant under the statute. Respondent Generix argues only

[10] Both the respondents and the Court of Appeals have suggested that if the term "new drug" referred to complete drug products, as opposed to active ingredients, then § 201(p)(2) of the Act would be superfluous. See 654 F. 2d, at 1116–1117. That section (set forth in n. 7, *supra*) establishes that before a drug may drop out of regulation, it must—in addition to being generally recognized among experts as safe and effective for the prescribed use—have been used to a material extent or for a material time other than in scientific investigations. The argument appears to rest on the premise that the only regulatory burden associated with being a new drug is the need to file a new drug application. Since an application must be filed *before* a drug can receive general public use, the argument is that nothing would be gained by deregulation because the only regulatory burden would have been sustained before one could be exempted from that burden. But the premise is flawed. Significant recordkeeping and reporting burdens are lifted when the "new drug" status terminates. See § 505(j) of the Act, 76 Stat. 782–783, 21 U. S. C. § 355(j). See also 21 CFR §§ 310.300–310.303 (1982).

[11] They argue (1) that legislative history suggests that the 1938 Congress rejected a product-by-product licensing system, (2) that in 1938 many pharmacists compounded their own pills with excipients of their choice and were not expected to file NDA's for each pill or every time they used a new excipient, (3) that between 1938 and 1968 the FDA advised drug manufacturers that certain generic products were not "new drugs" and therefore did not require NDA's to be marketed, (4) that the 1962 amendments reveal a congressional interest in promoting the availability of generic drugs in order to reduce the price of prescription drugs for consumers, (5) that in applying the 1962 amendments, the FDA took the position that, for some purposes, generic drug products were covered by NDA's of the pioneer

that its products are not new drugs under the theory that "drug" means "active ingredient"; it does not argue that its complete products—active ingredients and excipients together—are the same as previously approved products. The latter argument would, of course, have been unavailing on the facts before us; for the respondent has not questioned the District Court's finding of a reasonable possibility that its products are not bioequivalent to any previously approved products.[12] We thus do not reach the issue of whether two demonstrably bioequivalent products, containing the same active ingredients but different excipients, might under some circumstances be the same "drug."

In summary, a generic drug product is a "drug" within the meaning of § 201(g)(1) of the Act. Such a product is therefore a "new drug," subject to the requirements of § 505, until the product (and not merely its active ingredient) no longer falls within the terms of § 201(p). The judgment of the Court of Appeals is accordingly

Reversed.

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drugs that they copied, and (6) that since 1972 the FDA has used a "monograph" system to permit the marketing of over-the-counter drugs that meet prescribed standards and contain "suitable" excipients.

[12] Because the Government did not cross-appeal from the District Court's refusal to grant relief as to products containing prochlorperazine maleate and chlorthalidone, see n. 4, *supra*, we have no occasion to pass on the District Court's conclusion that the FDA has the burden of showing a "reasonable possibility" that a drug product is not bioequivalent to an approved product in order to enjoin distribution.